



1-26-04 Image 1654

Attorney's Office No. 9233-46

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Ekwuribe et al.
Application Serial No.: 10/075,097
Filed: February 13, 2002
For: METHODS OF TREATING DIABETES MELLITUS

Confirmation No.: 7253
Group Art Unit: 1654
Examiner: Anish Gupta

January 23, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

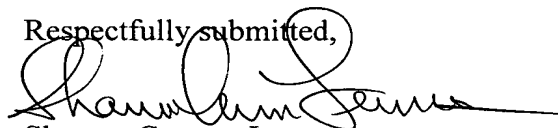
**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT
PURSUANT TO 37 C.F.R. § 1.97(b)**

Sir:

Attached is a form PTO-1449, together with a copy of each of the identified documents. It is requested that these documents be considered by the Examiner and officially made of record in accordance with the provisions of 37 C.F.R. §1.56 and Section 609 of the MPEP.

This Information Disclosure Statement is submitted in accordance with 37 C.F.R. §1.97(b), within three months of the filing date of the above-referenced application or before the mailing of a first Office Action on the merits, whichever event occurs last. Therefore, no fee is believed due. However, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,

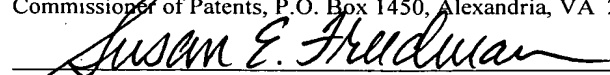

Shawna Cannon Lemon
Registration No. 53,888

Myers Bigel Sibley & Sajovec, P.A.
P. O. Box 37428, Raleigh, NC 27627
Telephone: (919) 854-1400
Facsimile: (919) 854-1401
Customer No. 20792

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Susan E. Freedman
Date of Signature: January 23, 2004

Substitute form 1449A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

1

of

1

**Complete if Known**

Application Number	10/075,097
Filing Date	02/13/2002
First Named Inventor	Nnochiri N. Ekwuribe
Group Art Unit	1654
Examiner Name	Anish Gupta
Attorney Docket Number	9233-46

U.S. PATENTS AND PATENT PUBLICATIONS

Examiner Initials*	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Number	Kind Code (if known)		
	1	US-5,889,153		Suzuki et al.	03/30/1999

OTHER NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T
	2	Aoki et al. "Chronic Intermittent Intravenous Insulin Therapy: A New Frontier in Diabetes Therapy" <i>Diabetes Technology & Therapeutics</i> 3(1):111-123 (2001)	
	3	Clement, Stephen "A Dose-Escalation Study of the Effects of Two Sequential Doses of Oral Modified Insulin on Blood Glucose Concentrations in Patients with Type 1 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 25, 2001) (Poster)	
	4	Francis et al. "Polyethylene Glycol Modification: Relevance of Improved Methodology to Tumour Targeting" <i>Journal of Drug Targeting</i> 3:321-340 (1996)	
	5	Guzman et al. "Effects of Fatty Ethers and Stearic Acid on the Gastrointestinal Absorption of Insulin" <i>PRHSJ</i> 9(2):155-159 (1990)	
	6	International Search Report, PCT/US02/04440, 12/23/2003	
	7	Lindsay et al. <i>The Acetylation of Insulin Biochem J.</i> 121:737-745 (1971)	
	8	Liu et al. "Glucose-Induced Release of Glycosylpoly(ethylene glycol) Insulin Bound to a Soluble Conjugate of Concanavalin A" <i>Bioconjugate Chem.</i> 8:664-672 (1997)	
	9	Mesiha et al. "Hypoglycaemic effect of oral insulin preparations containing Brij 35, 52, 58 or 92 and stearic acid" <i>J. Pharm. Pharmacol.</i> 33:733-734 (1981)	
	10	Michael et al. "Loss of Insulin Signaling in Hepatocytes Leads to Severe Insulin Resistance and Progressive Hepatic Dysfunction" <i>Molecular Cell</i> 6:87-97 (1999)	
	11	Moghaddam, Amir "Use of polyethylene glycol polymers for bioconjugations and drug development" <i>American Biotechnology Laboratory</i> pp. 42, 44 (July 2001)	
	12	Neubauer et al. "Influence of Polyethylene Glycol Insulin on Lipid Tissues of Experimental Animals" <i>Diabetes</i> 32:953-958 (October 1983)	
	13	Puskas et al. "Investigation of Chymotrypsin Digestion Profile of Orally Active Insulin Conjugate Him2" <i>AAPS PharmSci</i> 3(3) (2001) (Abstract)	
	14	Radakrishnan et al. "Stability and Physical Characteristics of Orally Active Amphiphilic Human Insulin Analog, Methoxy (Polyethylene Glycol) Hexanoyl Human Recombinant Insulin (HIM2)" <i>Proceed. Int'l. Symp. Control. Rel. Bioact. Mater.</i> 27:1038-39 (2000)	
	15	Shen et al. "(C) Means to Enhance Penetration; (3) Enhancement of polypeptide and protein absorption by macromolecular carriers via endocytosis and transcytosis" <i>Advanced Drug Del. Reviews</i> 8:93-113 (1992)	
	16	Sindelar et al. "A Comparison of the Effects of Selective Increases in Peripheral or Portal Insulin on Hepatic Glucose Production in the Conscious Dog" <i>Diabetes</i> 45:1594-1604 (1996)	
	17	Sirokman et al. "Refolding and proton pumping activity of a polyethylene glycol-bacteriorhodopsin water-soluble conjugate" <i>Protein Science</i> 12:1161-1170 (1993)	
	18	Torchilin, Vladimir P. "Immunoliposomes and PEGylated Immunoliposomes: Possible Use for Targeted Delivery of Imaging Agents" <i>Immunomethods</i> 4:244-258 (1994)	
	19	Wei et al. "A Poly(Ethylene Glycol) Water-soluble Conjugate of Porin: Refolding to the Native State" <i>Biochemistry</i> 34:6408-6415 (1995)	
	20	Xia et al. "Effects of polyoxyethylene chain length distribution on the interfacial properties of polyethylene glycol n-dodecyl ether" <i>Yingyong Huaxue</i> 2(4): 59-65 (1985) (Abstract)	
	21	Zalipsky et al. "Peptide Attachment to Extremities of Liposomal Surface Grafted PEG Chains: Preparation of the Long-Circulating Form of Laminin Pentapeptide YIGSR" <i>Bioconjugate Chem.</i> 6:705-708 (1995)	

Examiner Signature

Date Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.